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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,575	09/30/2003	Sudhir K. Sinha	P56885	2640

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EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 01/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/673,575	SINHA ET AL.	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-9,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1, 5-9, 21, and 22 are pending. The following Office Action is in response to Applicant's response dated December 12, 2005. Any rejection set forth in the NON-FINAL Office Action dated September 8, 2005 not reasserted in the following Office Action is considered withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1 and 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245).

Regarding Claim 1, Palmirotta et al. disclose a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 432, Column 2, Paragraphs 2,3); amplifying predetermined genomic DNA containing an Alu element by using primers (Page 432, Column 2, Paragraph 3) said Alu element being enriched in the human genome (Figure 1, Lane1) compared to non-human primates genomes (Figure 1, Lanes 9-15); and quantitating the human DNA by comparing the amplified DNA with a reference (Figure 1).

Palmirotta et al. does not specifically disclose the practice of an *intra*-ALU PCR.

Hoglund et al. disclose the practice of an intra-ALU PCR to identify somatic cell hybrids retaining human material (Abstract; Page 241, Column 1, Paragraph 5).

Based on the combined disclosures of the applied references, one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success practicing intra-ALU PCR in the methods of Palmirotta et al. The motivation to do so, provided by Hoglund et al., *would have been identify human DNA by amplifying*

ALU repeats (i.e. repeat element-mediated PCR). At the time of invention, the disclosure of Hoglund et al. clearly would have provided the instruction and motivation necessary for one of ordinary skill in the art to practice the methods as claimed. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the instant methods as claimed.

Regarding Claim 7, Palmirotta et al. disclose detecting the human DNA on an agarose gel stained with ethidium bromide (Figure 1).

2. Claims 1, 7, 21, and 22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245).

Regarding Claim 1, Carroll et al. disclose a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 38, Column 1, Paragraphs 2); amplifying predetermined genomic DNA containing an Alu element by using primers (Page 38, Column 2, Paragraph 1) said Alu element being enriched in the human genome (Abstract) compared to non-human primates genomes (Abstract); and quantitating the human DNA by comparing the amplified DNA with a reference (Page 38, Column 2, Paragraph 1).

Carroll et al. does not specifically disclose the practice of an *intra*-ALU PCR.

Hoglund et al. disclose the practice of an intra-ALU PCR to identify somatic cell hybrids retaining human material (Abstract; Page 241, Column 1, Paragraph 5).

Based on the combined disclosures of the applied references, one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success practicing intra-ALU PCR in the methods of Carroll et al. The motivation to do so, provided by Hoglund et al., *would have been identify human DNA by amplifying ALU repeats (i.e. repeat element-mediated PCR)*. At the time of invention, the disclosure of Hoglund et al. clearly would have provided the instruction and motivation necessary for one of ordinary skill in the art to practice the methods as claimed. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the instant methods as claimed.

Regarding Claim 7, Carroll et al. disclose detecting the human DNA on an agarose gel stained with ethidium bromide (Page 38, Column 2, Paragraph 1).

Regarding Claim 21, Carroll et al. disclose a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 38, Column 1, Paragraphs 2); amplifying predetermined genomic DNA containing an Alu element by using primers (Page 38, Column 2, Paragraph 1), said Alu element being present only in the human genome (Abstract); and quantitating the human DNA by comparing the amplified DNA with a reference (Page 38, Column 2, Paragraph 1).

Regarding Claim 22, Carroll et al. disclose a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 38, Column 1, Paragraphs 2); amplifying predetermined genomic DNA containing an young Alu element by using primers (Page 38, Column 2, Paragraph 1), said young Alu element being largely absent from non-human primates (Abstract); and quantitating the human DNA by comparing the amplified DNA with a reference (Page 38, Column 2, Paragraph 1).

3. Claim 5 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252).

Regarding Claim 5, the methods of Carroll et al. and Hoglund et al. have been outlined in the above rejections. Carroll et al. do not specifically disclose the *exact* primer sequences of SEQ ID NO: 3 and SEQ ID NO: 4, drawn to the Yb8 Alu subfamily.

Jurka discloses the entire Sb2 Alu subfamily sequence (Figure 1). The term "Sb2" is considered to older nomenclature of the Yb8 subfamily (See reference: Batzer

et al. "Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, Pages 3-6).

The *identical* primer sequence presented in SEQ ID NO: 3 (5'-CGAGGCGGGTGGATCATGAGGT-3' is contained in the sequence provided by Jurka (Figure 1) from nucleotides 48-69. Furthermore, the *identical* complement of the primer sequence (i.e. reverse primer) presented in SEQ ID NO: 3 (5'-TCTGTCGCCCAGGCCGGACT -3' is contained in the sequence provided by Jurka (Figure 1) from nucleotides 273-254.

Based on the disclosure of Jurka, one of ordinary skill in the art would have had a reasonable expectation of success using the primers presented in SEQ ID NO: 3 and SEQ ID NO: 4 to amplify a portion of the Yb8 Alu subfamily in the methods of Carroll et al. The motivation to so would have been 100% local similarity of the instant primers in the sequence provided by Jurka. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the methods as claimed.

4. Claim 6 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245), in further view of Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, Pages 3-6).

Regarding Claim 6, the methods of Carroll et al. and Hoglund et al. have been outlined in the previous rejections. Carroll et al. do not specifically disclose the *exact* primer sequences of SEQ ID NO: 5 and SEQ ID NO: 6, drawn to the Yd6 Alu subfamily.

Batzer et al. disclose that the younger subfamilies of Alu sequences contain individual members that are restricted to the human genome (Page 3, Column 2, Paragraph 1). In addition, they disclose that the "Y" subfamily is considered a "gold standard" since it has been previously identified as a subfamily by a number of different laboratories (Page 4, Column 2, Paragraph 2). Moreover, they disclose that *all* Alu repeats presently known to retropose differ from the Y subfamily consensus sequence by only a *few* additional diagnostic mutations, suggesting that the younger subfamilies of Alu repeats were ancestrally derived from the Y subfamily; therefore, young subfamilies are defined as lineages that descended from this gold standard (Page 4, Column 2, Paragraph 2; Page 5, Column 1, Paragraph 1).

Based on the disclosure of Batzer et al., one of ordinary of skill in the art at the time of invention would have had a reasonable expectation of success using the primers presented in SEQ ID NO: 5 and SEQID NO: 6 to amplify the Yd6 subfamily for use in the methods of Carroll et al. Hoglund et al. The motivation to do so, provided by Batzer et al., would have been not only that the Yd6 subfamily would have been expected to be enriched in the human genome, but that the Yd6 subfamily would behave in a similar fashion than the Yb8 subfamily due to the fact lineages were derived from a common ancestor and only differ by a few diagnostic mutations. It would have been *prima facie*

obvious to one of ordinary skill in the art at the time of invention to practice the methods as claimed.

5. Claims 8 and 9 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245), in view of Gelmini et al. ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Regarding Claims 8 and 9, the methods of Palmirotta et al. have been outlined in the above rejections. Palmirotta et al. does not specifically disclose the practice of a quantitative PCR system such as *Taq*Man.

Gelmini et al. disclose the practice of a quantitative PCR system using *Taq*Man chemistry (Figures 1,2,3; Table 1; Page 754, Columns 1,2). Furthermore, they highlight the advantages of using fluorogenic probes in PCR, such as the circumventing of post-PCR product quantitation procedures (Page 752, Column 2, Paragraph 2).

Based on the disclosure of Gelmini et al., one of ordinary one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success practicing the methods of Palmirotta et al. further comprising performing a quantitative

PCR system using *Taq*Man chemistry. The motivation to do so, provided by Gelmini et al., would have been to circumvent the need for post-PCR product quantitation procedures. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the methods as claimed.

6. Claims 8 and 9 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Hoglund et al. ("Isolation and characterization of radiation hybrids for human chromosome 12" Cytogenetic Cell Genetics. 1995. 69, Pages 240-245), in view of Gelmini et al. ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Regarding Claims 8 and 9, the methods of Carroll et al. have been outlined in the above rejections. Carroll et al. does not specifically disclose the practice of a quantitative PCR system such as *Taq*Man.

Gelmini et al. disclose the practice of a quantitative PCR system using *Taq*Man chemistry (Figures 1,2,3; Table 1; Page 754, Columns 1,2). Furthermore, they highlight the advantages of using fluorogenic probes in PCR, such as the circumventing of post-PCR product quantitation procedures (Page 752, Column 2, Paragraph 2).

Based on the disclosure of Gelmini et al., one of ordinary one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success practicing the methods of Carroll et al. further comprising performing a quantitative PCR system using *Taq*Man chemistry. The motivation to do so, provided by Gelmini et al., would have been to circumvent the need for post-PCR product quantitation procedures. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice the methods as claimed.

Response to Arguments- 35 USC § 103

Applicant's amendments and arguments with regard to the above rejections have been fully considered but they are not persuasive.

With regard to Claims 1, 7, 21, and 22, Applicant argues that the quantitation step is neither taught or suggested by Palmirotta et al. or Carroll et al. First, Claim 1 recites quantitation *by comparison* with a reference, which is clearly encompassed by the visual comparison one can make with an ethidium stained gel. Figure 1 of Palmirotta et al. clearly demonstrates a visual comparison with an ethidium stained gel. Carroll et al. disclose detecting the human DNA on an agarose gel stained with ethidium bromide (Page 38, Column 2, Paragraph 1). Moreover, Claim 7 of the instant application recites the quantitation step of the independent method as comprising detecting the human DNA on an agarose gel stained with ethidium bromide. It is not understood how Applicant can argue that the quantitation step is neither taught or suggested by Palmirotta et al. or Carroll et al. when Applicant clearly defines one

embodiment of the "quantitation step" as comprising the exact disclosure of the applied references.

Applicant further argues there is no suggestion or motivation to combine the applied references. Applicant specifically asserts that Hoglund teaches the use of a pair of inter-ALU primers, ALU3 and ALU5. Applicant is correct is asserting that Hoglund teaches inter-ALU PCR, however, this amplification is performed *after* an intra-ALU (i.e. amplification of an ALU sequence within an ALU element) (See Abstract; Page 241, Column 1, Paragraph 5) amplification. Furthermore, Hoglund specifically discloses performing intra-ALU for the purpose of identifying human DNA, which provides the instruction and motivation necessary for one of ordinary skill in the art to practice the methods as claimed.

With regard to Claim 5, Applicant argues that 100% local similarity does not suggest the combination of the applied references. Since Jurka et al. clearly discloses successful amplification with the primer sequences recited in Claim 5, one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success using the primers presented in SEQ ID NO: 3 and SEQ ID NO: 4 to amplify a portion of the Yb8 Alu subfamily in the methods of Carroll et al.

With regard to Claim 6, Applicant did not provide any reasoning as to why the rejection is improper. As such, the rejection is maintained.

With regard to Claims 8 and 9, it is noted that the Office Action dated September 8, 2005 did contain a typographical error with regard to Claims 8 and 9. Applicant states that the Office action did provide reasoning for the rejection of Claim 9. The

rejection of Claim 9 encompasses the rejection of Claim 8. Applicant did not provide any reasoning as to why the rejection is improper. As such, the rejection of **Claims 8 and 9** is maintained.

Conclusion

No claims are allowed. No claims are free of the prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-

272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

12/29/05

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KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

1/3/06